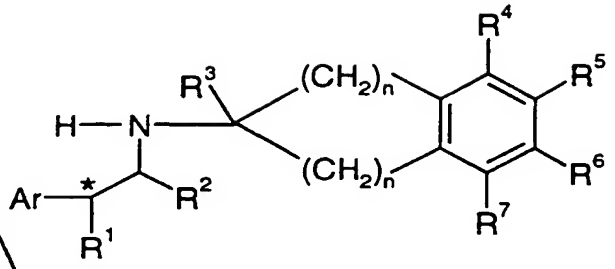
Claims

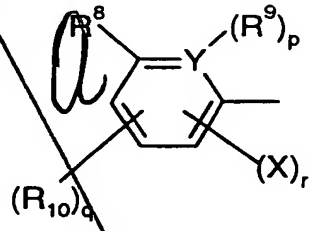
1. A compound of formula



I

in free or salt or solvate form, where

Ar is a group of formula



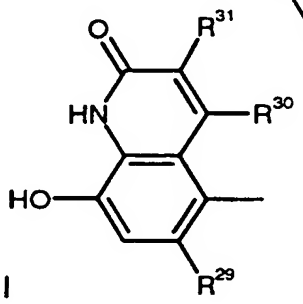
II

R^1 is hydrogen, hydroxy, or alkoxy,
R^2 and R^3 are each independently hydrogen or alkyl,
R^4, R^5, R^6 and R^7 are each independently hydrogen, halogen, cyano, hydroxy, alkoxy, aryl, alkyl, alkyl substituted by one or more halogen atoms or one or more hydroxy or alkoxy groups, alkyl interrupted by one or more hetero atoms, alkenyl, trialkylsilyl, carboxy, alkoxycarbonyl, or $-CONR^{11}R^{12}$, where R^{11} and R^{12} are each independently hydrogen or alkyl, or R^4 and R^5, R^5 and R^6, or R^6 and R^7 together with the carbon atoms to which they are attached denote a carbocyclic or heterocyclic ring,
R^8 is halogen, $-OR^{13}$, $-CH_2OR^{13}$ or $-NHR^{13}$ where R^{13} is hydrogen, alkyl, alkyl interrupted by one or more hetero atoms, $-COR^{14}$, where R^{14} is hydrogen, $-N(R^{15})R^{16}$, alkyl or alkyl interrupted by one or more hetero atoms, or aryl and R^{15} and R^{16} are each independently hydrogen, alkyl or alkyl interrupted by one or more hetero atoms, or R^{13} is $-C(=NH)R^{17}$, $-SOR^{17}$ or $-SO_2R^{17}$ where R^{17} is alkyl or alkyl interrupted by one or more hetero atoms, and R^9 is hydrogen, or R^8 is $-NHR^{18}$ where $-NHR^{18}$ and R^9, together with the carbon atoms to which they are attached, denote a 5- or 6- membered heterocycle,

R^{10} is $-OR^{19}$ or $-NHR^{19}$ where R^{19} is hydrogen, alkyl, alkyl interrupted by one or more hetero atoms, or $-COR^{20}$, where R^{20} is $-N(R^{21})R^{22}$, alkyl or alkyl interrupted by one or more hetero atoms, or aryl, and R^{21} and R^{22} are each independently hydrogen, alkyl or alkyl interrupted by one or more hetero atoms,
X is halogen or halomethyl or alkyl,
Y is carbon or nitrogen,
n is 1 or 2,
p is zero when Y is nitrogen or 1 when Y is carbon,
q and r are each zero or 1, the sum of q+r is 1 or 2; and
the carbon atom marked with an asterisk* has the R or S configuration, or a mixture thereof, when R^1 is hydroxy or alkoxy.

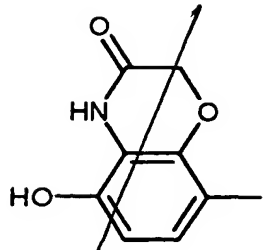
2. A compound according to claim 1, in which Ar is a group of formula II in which
Y is carbon,
R^8 is $-NHR^{18}$ and $-NHR^{18}$ and R^9 together denote
a group of formula $-NH-CO-R^{23}-$ where R^{23} is an alkylene, alkenylene or alkyleneoxy group,
a group of formula $-NH-SO_2-R^{24}$ where R^{24} is an alkyleneoxy group,
a group of formula $-NH-R^{25}(COOR^{26})-$ where R^{25} is an alkylene or alkenylene group and R^{26} is alkyl, or
a group of formula -NH-CO-NH- or -NH-CO-S-,
R^{10} is $-OR^{19}$, where R^{19} is as defined in claim 1,
X is alkyl,
p is 1, q is 1 and r is zero or 1.

3. A compound according to claim 2, in which Ar is a group of formula III, IV, V, VI or VII :

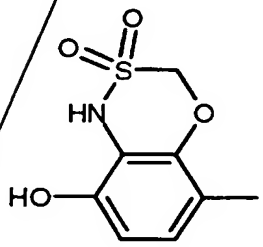


III

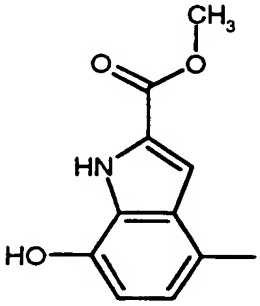
in which R^{29}, R^{30} and R^{31} are each independently hydrogen or C_1-C_4-alkyl



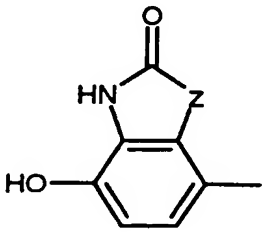
IV



V



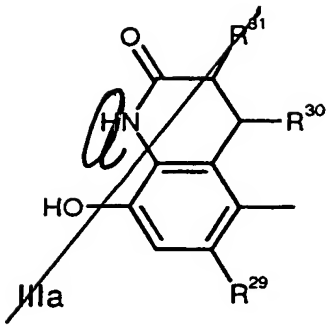
VI



VII

in which Z is -O-, -NH- or -S-.

4. A compound according to claim 1, in which Ar is a group of formula

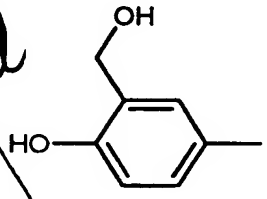


IIIa

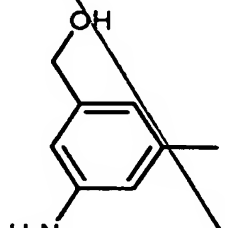
where R^{29}, R^{30} and R^{31} are each independently hydrogen or C_1-C_4-alkyl.

5. A compound according to claim 1, in which Ar is a group of formula II in which Y is carbon, R^8 is $-CH_2OR^{13}$ where R^{13} is hydrogen, C_1-C_4-alkyl, or C_1-C_4-alkoxy-C_1-C_4-alkyl, R^9 is hydrogen, R^{10} is $-OR^{19}$ where R^{19} is hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_1-C_4-alkyl or R^{10} is $-NHR^{19}$ where R^{19} is hydrogen, C_1-C_4-alkyl or $-COR^{20}$ where R^{20} is C_1-C_4-alkyl, C_6-C_{10}-aryl or $-N(R^{21})R^{22}$ where R^{21} and R^{22} are each independently hydrogen or C_1-C_4-alkyl, p and q are each 1 and r is zero; or a group of formula II in which Y is nitrogen, R^8 is $-CH_2OR^{13}$ where R^{13} is hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_1-C_4-alkyl, R^{10} is $-OR^{19}$ where R^{19} is hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy- C_1-C_4-alkyl, p and r are zero and q is 1.

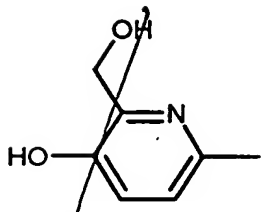
6. A compound according to claim 5, in which Ar is a group of formula XII, XIII or XIV



XII



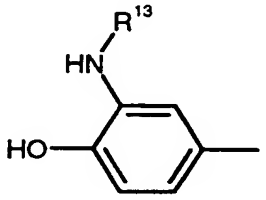
XIII



XIV

7. A compound according to claim 1, in which Ar is a group of formula II in which Y is carbon, R^8 is $-NHR^{13}$ where R^{13} is hydrogen, C_1-C_{10} alkyl, C_1-C_{10} alkyl interrupted by 1 to 3 hetero atoms, $-COR^{14}$ where R^{14} is hydrogen, C_1-C_{10}-alkyl or C_1-C_{10}-alkyl interrupted by 1 to 3 hetero atoms, or R^{13} is $-C(=NH)R^{17}$, $-SOR^{17}$ or $-SO_2R^{17}$ where R^{17} is C_1-C_{10}-alkyl or C_1-C_{10}-alkyl interrupted by 1 to 3 hetero atoms, R^9 is hydrogen, R^{10} is $-OR^{18}$ where R^{18} is hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_1-C_4 alkyl, p and q are each 1 and r is zero.

8. A compound according to claim 7, in which Ar is a group of formula XV



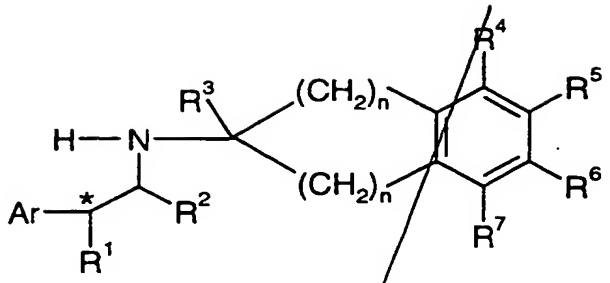
XV

9. A compound according to any one of the preceding claims, in which R^4, R^5, R^6 and R^7 are each hydrogen or are such that the benzene ring to which they are attached is symmetrically substituted.

10. A compound according to claim 1, in which Ar is a group of formula III, IV, V, XII or XV, R^1 is hydroxy, R^2 and R^3 are hydrogen, and R^4 and R^7 are identical and are each hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy, and either R^5 and R^6 are identical and are each hydrogen, C_1-C_4-alkyl, C_1-C_4-alkoxy or C_1-C_4-alkoxy-C_1-C_4-alkyl, or R^5 and R^6 together denote $-(CH_2)_4-$ or $-O(CH_2)_2O-$, in free or salt or solvate form.

11. A compound according to claim 10, in which the carbon atom in formula I marked with an asterisk * has the R configuration.

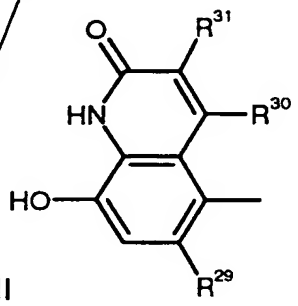
12. A compound of formula



I

in free or salt or solvate form,

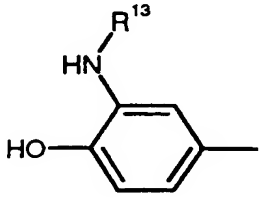
(A) wherein Ar is a group of formula



III

in which R^{29}, R^{30} and R^{31} are each H, R^1 is OH, R^2 and R^3 are each H and
(i) n is 1, and R^4 and R^7 are each CH_3O- and R^5 and R^6 are each H; or
(ii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3CH_2-; or
(iii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3-; or
(iv) n is 1, and R^4 and R^7 are each CH_3CH_2- and R^5 and R^6 are each H; or
(v) n is 1, and R^4 and R^7 are each H and R^5 and R^6 together denote -$(CH_2)_4$-; or
(vi) n is 1, and R^4 and R^7 are each H and R^5 and R^6 together denote -$O(CH_2)_2O$-; or
(vii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each $CH_3(CH_2)_3$-; or
(viii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each $CH_3(CH_2)_2$-; or
(ix) n is 2, R^4, R^5, R^6 and R^7 are each H; or
(x) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3OCH_2-; or

(B) wherein Ar is a group of formula



XV

in which R^{13} is H, R^1 is OH, R^2 and R^3 are each H, R^4 and R^7 are each H and R^5 and R^6 are each H and n is 1; or

(C) which is a compound selected from 8-hydroxy-5-[1-hydroxy-2-(indan-2-ylamino)-ethyl]-1H-quinolin-2-one, 5-[2-(5,6-dimethoxy-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, 5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-3-methyl-1H-quinolin-2-one, 5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-methoxymethoxy-6-methyl-1H-quinolin-2-one, 5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-6-methyl-1H-quinolin-2-one, 8-hydroxy-5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-3,4-dihydro-1H-quinolin-2-one, N-{2-hydroxy-5-[(R)-1-hydroxy-2-(2,5,6-trimethyl-indan-2-ylamino)-ethyl]-phenyl}-formamide, 5-[(R)-2-(5,6-diethyl-2-methyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, (S)-5-[2-(4,7-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-1H-quinolin-2-one hydrochloride, 5-[(R)-1-hydroxy-2-(6,7,8,9-tetrahydro-5H-benzocyclohepten-7-ylamino)-ethyl]-1H-quinolin-2-one hydrochloride, (R)-5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-1H-quinolin-2-one hydrochloride, N-{5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-2-hydroxy-phenyl}-formamide, 4-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-2-dimethylamino-phenol hydrochloride, 4-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-2-methylamino-phenol hydrochloride, N-{5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-2-hydroxy-phenyl}-methanesulfonamide hydrochloride), (R)-8-hydroxy-5-[(S)-1-hydroxy-2-(4,5,6,7-tetramethyl-indan-2-ylamino)-ethyl]-1H-quinolin-2-one, 8-hydroxy-5-[(R)-1-hydroxy-2-(2-methyl-indan-2-ylamino)-ethyl]-1H-quinolin-2-one, 5-[2-(5,6-diethyl-indan-2-ylamino)-ethyl]-8-hydroxy-1H-quinolin-2-one, 8-hydroxy-5-[(R)-1-hydroxy-2-(2-methyl-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]naphthalen-2-ylamino)-ethyl]-1H-quinolin-2-one, 5-[(S)-2-(2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]naphthalen-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, N-{2-hydroxy-5-[(R)-1-hydroxy-2-(2-methyl-indan-2-ylamino)-ethyl]-phenyl}-methanesulfonamide), ethanesulfonic acid {2-hydroxy-5-[(R)-1-hydroxy-2-(2-methyl-indan-2-ylamino)-ethyl]-phenyl}-amide, propane-1-sulfonic acid {2-hydroxy-5-[(R)-1-hydroxy-2-(2-methyl-indan-2-ylamino)-ethyl]-phenyl}-amide, N-{5-[2-(2-ethyl-indan-2-ylamino)-1-hydroxy-ethyl]-2-hydroxy-phenyl}-methanesulfonamide, or N-{2-hydroxy-5-[(R)-1-hydroxy-2-(2,5,6-trimethyl-indan-2-ylamino)-ethyl]-phenyl}-methanesulfonamide.

13. A pharmaceutical composition comprising a compound according to any one of the preceding claims, optionally together with a pharmaceutically acceptable carrier

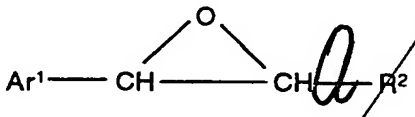
14. Use of a compound according to any one of claims 1 to 12 for the preparation of a medicament for the treatment of a condition which is prevented or alleviated by activation of the β2-adrenoreceptor.

15. Use of a compound according to any one of claims 1 to 12 for the preparation of a medicament for the treatment of an obstructive or inflammatory airways disease.

16. A process for the preparation of a compound of formula I in free or salt or solvate form comprising:

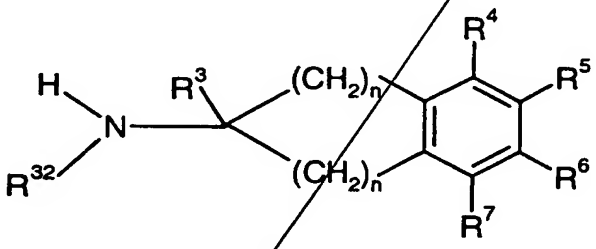
(a) for the preparation of a compound where R^1 is hydroxy, either

(i) reacting a compound of formula



XVI

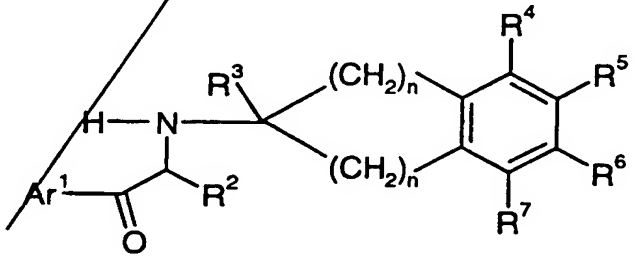
with a compound of formula



XVII

where Ar^1 is Ar as defined in claim1 or a protected form thereof, R^2, R^3, R^4, R^5, R^6, R^7 and n are as defined in claim 1 and R^{32} is hydrogen or an amine-protective group, or

(ii) reducing a compound of formula



XVIII

where Ar^1 is Ar as defined in claim 1 or a protected form thereof, R^2, R^3, R^4, R^5, R^6 and R^7 are as defined in claim 1, to convert the indicated keto group into -CH(OH)-; or

(b) for the preparation of a compound where R^1 is hydrogen, reducing a corresponding compound of formula I where R^1 is hydroxy; or

(c) for the preparation of a compound of formula I where R^1 is alkoxy, either (i) O-alkylating a corresponding compound of formula I where R^1 is hydroxy or (ii) reacting a corresponding compound having a leaving moiety instead of R^1 with an alcohol of formula R^1H where R^1 is alkoxy;

and, optionally, converting a resultant compound of formula I in protected form into a corresponding compound in unprotected form;

and recovering the resultant compound of formula I in free or salt or solvate form.